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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/560,179 | 12/09/2005 | Shigeru Akasofu | 09857/0203535-US0 | 7982 |

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| EXAMINER | |
|---|---|
| CLAYTOR, DEIRDRE RENEE | |
| ART UNIT | PAPER NUMBER |
| 1617 | |

| MAIL DATE | DELIVERY MODE |
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| 09/17/2008 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/560,179 | AKASOFU ET AL. | |
| | Examiner | Art Unit | |
| | Renee Claytor | 1617 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *24 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *13 and 18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13, 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Request for Continued Examination*

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/24/2008 has been entered.

### *Response to Arguments*

Applicants argue that the 35 USC 112 rejection is improper because the Examiner construes the claims based on an unduly broad definition of "protection". The Applicants point out that the definition of "protection" in the specification only calls for preventing "cell death" and the "lowering neuronal function".

In response to the above argument, it is noted that the term "protecting" encompasses prevention as well by Applicant's definition in the specification. As previously discussed, there is no teaching in the specification that there is complete prevention of damage to neurons. Though Applicants define "protecting neurons" as preventing cell death and lowering neuronal function, it does encompass prevention. Further, the examples do not teach full prevention of Aβ toxicity but only decreased toxicity. Therefore, the claims are examined as they read on prevention and the 35 USC 112 rejection is maintained.

Applicants argue that the 35 USC 102 rejection is improper because Emilien does not disclose or suggest a method of protecting neurons by administering the claimed compound but merely teaches various drugs for treating Alzheimer's disease (AD). Applicants assert that Emilien is silent with regard to whether donepezil would protect neurons from damage induced by Aβ toxicity.

In response to the above arguments, it is again noted that it is well known in the art, and is taught by Michaelis that the generation, aggregation and deposition of Aβ plaques is associated with AD. Accordingly, because it is known in the art that donepezil treats AD, there would be an overlapping patient population because AD is associated with deposition of Aβ plaques as well as the cholinergic system. Inherently, donepezil would inherently treat neurons in the treatment of AD.

Because the rejections are maintained, this Office Action is being made final.

***Claim Rejections – 35 U.S.C. §112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13 and 18 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating Aβ aggregation in cholinergic neurons in the CNS, does not reasonably provide enablement for protecting (interpreted by the Examiner to mean prevention) all neurons of the CNS. The specification does not

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

**1) The nature of the invention and breadth of the claims:** The nature of the invention and breadth of the claims are drawn to a method of protecting neurons of the central nervous system, comprising administration of donepezil.

**2) The presence or absence of working examples and the amount of direction or guidance presented:** In the instant case, no working examples are presented in the specification as filed showing how to prevent Aβ aggregation in cholinergic neurons. The specification outlines experiments showing that donepezil decreases Aβ aggregation in cholinergic neurons. Figures 8-10 shows that the addition of donepezil decreases Aβ aggregation in cholinergic neurons, proving that donepezil is effective at reducing Aβ aggregation and not for prevention of Aβ aggregation.

**3) The state of the prior art:** The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more details as to how to make and use invention in order to be enabling. >See, e.g., Chiron Corp. v. Genentech Inc., 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1326 (Fed. Cir. 2004).

The state of the art regarding treating Aβ aggregation in PC12 shows that administration of donepezil decreases Aβ toxicity (see Figure 1) but does not show total inhibition on toxicity induced by Aβ (see NeuroReport (1998) 9, 1519-1522). Therefore, the use of donepezil is not art recognized as preventing Aβ toxicity.

**4) The quantity of experimentation necessary**: Claims 13 and 18 read on a method of protecting neurons of the central nervous system, comprising administration of donepezil. As discussed above, the specification fails to provide sufficient support for completely preventing disorders, such as Aβ toxicity in neurons. Applicant fails to provide information sufficient to practice the claimed invention, absent undue experimentation. Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

***Claim Rejections – 35 U.S.C. § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 13 and 18 rejected under 35 U.S.C. 102(b) as being anticipated by Emilien et al. (Arch Neurol 57 (2000) pgs. 454- 459) as evidenced by Michaelis (JPET 304 (2003) 897-904).

Emilien et al. teach that 1-benzy-4-L(5,6-dimethyloxy-1-indanone)-2-yl]methylpiperidine (herein after termed donepezil) is an acetylcholinesterase, FDA approved therapy for Alzheimer's disease (see pg. 455, Col. 2).

The treatment of a disorder in a neuron that is induced by Aβ toxicity is inherently taught by Emilien et al. According to Michaelis the generation, aggregation and deposition of amyloid (Aβ) plaques in the brain is associated with Alzheimer's disease in the brain (pg. 898, first paragraph in second column). Aggregation of Aβ in the vicinity of neurons leads to toxic cellular events and is regarded as the culprit responsible for neurodegeneration (pg. 900, first paragraph in first column; pg. 901, second paragraph in first column). Therefore, because donepezil treats Alzheimer's, it would necessarily treat Aβ toxicity as well.

### *Conclusion*

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

### *Contact Information*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Renee Claytor whose telephone number is (571)272-8394. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Renee Claytor

/SREENI PADMANABHAN/
Supervisory Patent Examiner, Art Unit 1617